

IN THE SPECIFICATION

Please **amend** the paragraph on page 1 between lines 7 and 10 with the following:

This application claims priority to commonly assigned Provisional Application Serial No. 60/455,970~~60/445,970~~ filed March 19, 2003 and International Patent Application Number PCT US2004/008558 filed on March 19, 2004. International Application No. PCT/US00/12287, filed 05 May 2000 is incorporated herein by reference.

Please **amend** the paragraph on page 3 between lines 13 and 25 with the following:

A fluid containing materials under test flows through the array between the surfaces forming the mirror elements, the material having an affinity for a capturing material in one or more array cells. Instead of a fluid (gas or liquid with particles or fluid component~~secomenets~~ under test) a solid of appropriate transparency may be tested. These materials will be bound to the capturing material of that cell having such an affinity changing the resonant properties of the resonant cavity formed between the mirror surfaces in that cell. The result will be a change in the light received by the corresponding CCD pixels. That change can be detected by processing electronics correlating the position of the change, its nature and the known affinity of that particular resonant cavity cell.

Please **amend** the paragraph on page 5 between lines 6 and 21 with the following:

Fig. 1 illustrates an optical control system according to the invention in which a wavelength tunable laser 1, which may be an Aristu MNG638A provides output radiation typically in the vicinity of 1560 nanometers (15,600 Angstroms) to a single mode optical fiber 2. Radiation in the fiber 2 is applied to an optical attenuator 3, which may be an Agilent 85156A. The attenuator provides dynamic adjustment consistency to promote the operation of the system as a whole as described below. In order to provide beam cleaning which insures a ~~Gaussian~~Gaussian distribution to the spatial intensity profile of the beam, the output of the attenuator 3 is applied through a long coil of single mode fiber 4, typically 5Km. The thus cleaned light is applied through a fiber collimator 5 which uses an antireflective coated objective at 1550 nanometers. The collimator produces a 1mm beam, the diameter being measured between half maximum intensity points.

Please **amend** the paragraph on page 6 between lines 1 and 6 with the following:

The detection system comprises a cavity 16 formed between first and second reflecting surfaces 14 and 15 separated by a space ~~16~~—within which a standing wave is generated by the radiation in beam 11. That radiation is applied through a lower support 17, aperture 18 into a lower or first stage 19 through a further aperture 20.

Please **amend** the paragraph on page 6 between lines 7 and 11 with the following:

The second reflective surface 15 is supported by a second stage 21 supported by a second support 22. ~~Adjusters~~~~Micrometers~~ 23 and 24 allow adjustment of the first stage 19 with respect to the first support 17 while a micrometer 25 provides a similar function for the second stage 21 with respect to the support 22.

Please **amend** the paragraph on page 6 between lines 12 and 32 with the following:

The light in beam 11 creates a standing wave pattern in thea cavity 16, particularly one dependent upon the characteristics of a capturing material applied to each cell in an array on the mirror 14, all as described more completely herein below. Light of an intensity dependant upon the degree of resonance within each cell travels in a beam 30 through a focusing lens 31 to a camera 32, typically by reflection from a 45° mirror 33. The camera 32, which may be a Sensors Unlimited SU128-1.7R camera having a InGaAs sensor with pixels in a 128 x 128 array, receives that light. Typically, each cell will be imaged onto one or more pixels in the array of camera 32. The image from camera 32 is read into a computer 34 to an image acquisition card 35, which may typically be a National Instrument NI-PCI1422. The computer 34 has a controller card 36, typically a GPIB card, which applies control signals to the tunable laser 1. The card 36 also operates through a piezoelectric controller 37 to control piezoelectric actuators on the adjusters 23 and 24, typically placed at their tips where they ~~join~~joint the first stage 19. The computer 34 may have an input/output interface 38 for communication with users, networks, printers display and other typical computer accessories.

Please **amend** the paragraph on page 7 between lines 1 and 11 with the following:

The computer maintains a feedback loop through the piezoelectric controller 37 on the ~~adjusters~~actuators 23 and 24 via the camera 32 to sense fringe patterns in the optical image received and processed by the camera 32 which are an indication of an out of parallel condition between the stages 19 and 21, using known minimization techniques, the piezoelectric drives are operated to minimize those fringing elements thereby obtaining a parallel condition of the stages 19 and 21. The piezo elements are also operable by the computer to vary the spacing between reflectors as an alternative or complementary to wavelength scanning of the laser radiation.

Please **amend** the paragraph on page 7 between lines 12 and 18 with the following:

A heating element 42 operates with a heat control unit 43 which may or may not have a connection to computer 34 in order to maintain or control the temperature between the stages 19 and 21 and in particular within the cavity region 16 where standing wave patterns are created by the incident illumination. This heat control accomplishes the function of avoiding dynamic changes on the mirrors during testing.



Please **amend** the paragraph on page 7 between lines 19 and 24 with the following:

The computer 34 is programmed to process the image data from each pixel received by the camera 32 in order to determine the thickness between the reflectors 14 and 15 in each cell, representative of the binding of material flowed through the intermirror, cavity region 16 for biologic or chemical assay purposes. This process includes the steps of:

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Please **amend** the paragraph between line 4 on page 8 and line 8 on page 9 with the following:

In the operation of the feedback control of mirror alignment, if there is an angle between the two mirrors 14 and 15, such that the distance between them changes by more than a half wavelength, the cavity 16 will be resonant in some places and non-resonant at others. Everywhere the resonance condition is satisfied, the camera 32 and computer 34 will see bright spots on the camera monitoring transmission. For a perfectly flat mirror at an angle, this amounts to horizontal lines indicating equal cavity spacing where resonance is satisfied. As one of the angles is tuned, the lines grow closer together or farther apart. Closer together, indicates that the angle perpendicular to the lines is growing steeper. As one of the adjustment knobs is tuned far to one end, the lines will grow increasing close together and increasing perpendicular to that angle. If the same knob is turned the other direction, the lines grow closer and less perpendicular to that angle. As the knob is kept turning, the lines will go ~~through~~through an optimal position after which they will again start to grow closer together and more perpendicular to the direction of angle change. By adjusting very carefully, one can tune to that optimal position where the lines would start contracting again if there was movement in either direction of the tuning knob, and where the lines are actually parallel to the direction of the angle adjustment. This means that in this direction, the surface is completely flat. The same is repeated for the other direction. Once the other direction is done, the first one has probably moved a bit due to vibration from handling

of the system, so an iterative approach may be needed to some extent. Wavelength changes move the lines but not their orientation, and the spacing between lines only changes slightly due to wavelength and can be taken into account by simply realizing that it was due to wavelength not angle change. Most often, we can not get to the point that the surface is completely lit due to surface curvature. A circle is eventually seen instead of the whole screen going bright, because the surface is curved and satisfying the resonant condition at only places on the circle, no ~~matter~~matter how parallel the mirrors 14 and 15 are. When this circle is visible, the mirrors 14 and 15 are reasonably parallel and tuning can stop.

Please **amend** the paragraph on page 9 between lines 9 and 14 with the following:

The peizo / computer control can take over this function and it allows much finer adjustment, making it easier to tune. The peizos do not~~do not~~ disturb the system like the hand of a human operator ~~does~~ on the adjusters 23 and 24 ~~micrometer~~ does. It is then possible to control the system to keep the mirrors 14 and 15 parallel throughout the operation of the biosensor.

Please **amend** the paragraph on page 9 between lines 15 and 27 with the following:

Fig. 2 illustrates an array of cells 80, typically those which may be applied to the surface of mirror 14 in bio or protein chips of known design. Hundreds of thousands or even millions of cells 80 can be provided in the mirror 14 within the cavity region ~~16channel 10~~. These cells 80, as noted above, are typically imaged into one or more pixels 82 of a photodetector array 84 in Fig. 3 within the multi-channel detector 30. Alternatively, the pattern illustrated by Fig. 3 can represent the pattern of light emitters such as from laser diodes. The memory associated with processor 34 will correlate one or more of the pixels 82 of the photodetector array 84 to corresponding cellscavities 80 and the particular molecular affinity of the material bonded to the mirror 14, typically to several angstroms in depth.

Please **amend** the paragraph on page 10 between lines 3 and 9 with the following:

Light from the laser 1 provides wavefronts 100 which pass into the cavity region 16~~1600~~ through mirror 12 and are reflective within the cavity 16 by the reflectance of the mirrors 14 and 15 to the wavelength and the incident radiation 100. As molecules in the flow through cavity~~channel~~ 16 bind to the capturing material~~region~~ 90, the wavelength response will shift from an original array 102 in Fig. 4A to a shifted wavelength response 104 in Fig. 4B.

Please **amend** the paragraph on page 10 between lines 10 and 18 with the following:

Fig. 5 illustrates in greater detail the mirrors 14 and 15 as consisting of a plurality of alternating silicon and silicon dioxide dielectric layers 106 and 108, respectively. As illustrated in Fig. 5, the surface of the first mirror-layer 14 will typically be terminated with an extra silicon dioxide layer 108 causing a standing wave pattern 110 within the cavity region 16 illustrated in Fig. 5 to have a peak 112 at the outer wall of the layer 108. This maximizes the effectiveness and sensitivity of the detection system of the present invention.



Please **amend** the paragraph between line 19 on page 13 and line 23 on page 14 with the following:

Processing data: The resulting wavelength response curve for each pixel was then low pass filtered with a 5 samples/nm cutoff. The data ~~were~~was then broken down into groups of 9 waveforms taken from 3x3 sets of neighboring pixels. The groupings were made so that they overlap by 1 row or column of pixels with neighboring groups of 3x3. Within each 3x3 group, the 9 wavelength response curves were cross correlated to each other. The peak of the cross-correlations indicates the shift between those two waveforms. Nine (9) waveforms cross correlating with each other produces 81 correlations, including 9 auto correlations, which leads to 72 shifts describing the relative position of each pixel with respect to the other 8 pixels. This information is heavily redundant. A linear systems over determined problem was setup and solved to find 8 shifts for 8 of the pixels relative to the top left most pixel which was given the shift of zero. This was done for all of the overlapping groups of 3x3 pixels. The top left most group of 3x3 pixels was designated to have a zero overall offset. The offset of the other 3x3 groupings relative to this first 3x3 group was then determined. The offset for each of the 3x3 groupings was found from solving a linear systems over determined problem as well, where the equations are derived from the fact that the 3x3 groupings overlap by columns and rows that must be consistently the same height. The solution of this problem provided an overall offset for each of the 3x3 groups. The final result is a mesh where the height of each pixel indicates the shift between its wavelength response and that of

the upper left most pixel on the camera. There are two key advantages to this technique. First, only local waveforms are ever correlated directly. This is important because the wavelength response drifts in overall shape across the sensor surface due to inhomogeneous illumination and curvature of the mirror structure. Comparing only local pixels, we are more assured that the resonant waveform has the same shape and its only the shift we are measuring. Secondly, by comparing each pixel to 8 of its neighbors, redundancy is gained which is used to improve the accuracy of the observed shift over a correlation done between just two pixels.